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Utility of *p*-Acetamidobenzoyl Prop-2-enoic Acid in the Synthesis of New α-Amino Acids and Using Them as Building Blocks in Heterocyclic Synthesis

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THE PRESENT work deals with the generation and synthesis of different unnatural amino acid derivatives *via* treatment of 3-(4-acetamidobenzoyl)-prop-2-enoic acid with 5-aryl-2- amino 1, 3, 4 thiadiazole, 3, 5-dimethyl pyrazole and barbituric acid to afford the product of conjugate addition acids (1) respectively. Additionally, the adduct 1 are used as key starting materials to synthesize some heterocycles include pyridazene , furanone and oxazine derivatives. The antimicrobial screening of some of the synthesized compounds was done using the agar diffusion assay

Keywords: 3-Acetamidobenzoyl prop-2-enoic acid, Pyrazole thiadiazole , Phthalimide , Barbituric acid, Furanone, Pyridazine and Oxazine.

Amino acids are the smallest unit of protein and are useful components in a variety of metabolisms. There are more than advantages of taking amino acids dietary supplements come from their many useful biological activities. *In vitro* data[(1)] about amino acids include muscle protein maintenance, potentiation of immune function, affecting neuronal activities in the brain, tissue repair acceleration, protecting liver from toxic agents, pain relief effect, lowering blood pressure, modulating cholesterol metabolism, stimulating insulin of growth hormone secretion and so on . It is important to be aware that they are part of complex pathway and biological systems. Amino acids have proven to play a significant role in the synthesis of novel drug candidate with the use of non-proteinogenic and unnatural amino acids[(2-9)]. Thus, we reported the reactions of 3(*p*-acetamidobenzoyl) 2-(2-amino 5-aryl thiadiazole) propionic acids 1 with N_2H_4, phenylhydrazine, hydroxyl amine and acetic anhydride to give the corresponding pyridazinone, oxazinone and furanone derivative, respectively aiming to afford some interesting heterocyclic compounds with non-mixing and mixing system .

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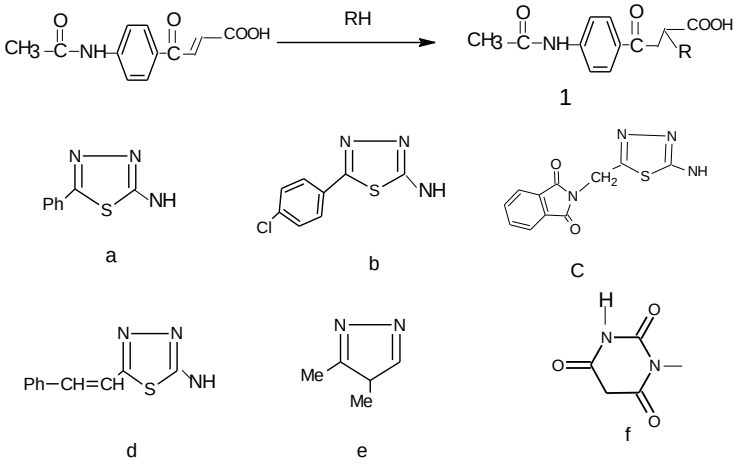
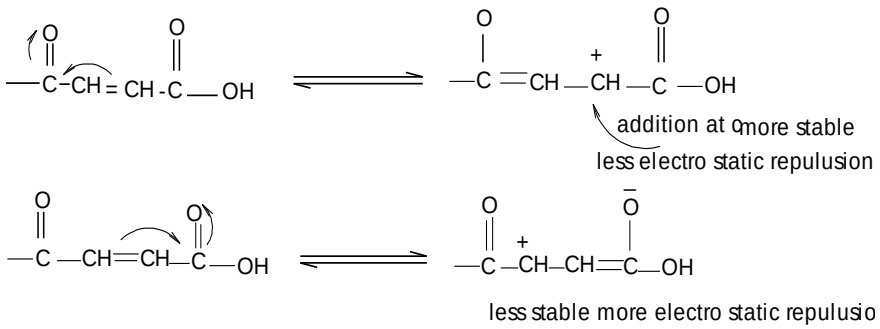
Results and Discussion

When 3 (*p*-acetamidobenzoyl) prop -2- enoic acid was allowed to react with 2-amino 5-aryl thiadiazole derivatives, it afforded the product of conjugate addition , 3 (*p*-acetamidobenzoyl) -2-(5-aryl 2-thiadiazolyl amino) propanoic acids as α-amino acid types that differ in biological activity by differing the aryl groups (Table 1) (Scheme1). IR spectra of acids 1 exhibit strong absorption at (1695 – 1630) cm^{-1} CO for acid and ketone groups in addition to υ CO in case of 1_c and 1_f at (1770 – 1712) and (1615) corresponding to phthalimido and barbiturate moieties, respectively.



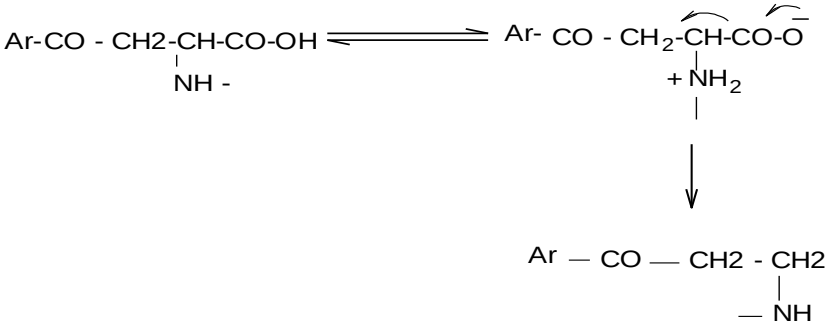
Moreover, reactivity of C_2 in 3-aroyl propio-2-enoic acids[10-11] allows aza-michael addition by 2ry amine, *e.g* 4,5-dimethyl pyrazole and barbaturic acid . The preference for nucleophilic addition at C_2 is discussed in terms of a) stability of resonance forms of the acrylic starting material . The relative stabilities of the alternative structures of the primary zwitter ionic adduct indicate that the negative charge on the enolate moiety resulting from addition at C_2 to be more delocalized than C_3 as below:



b) An electronic influence of the *p*-acetamidophenyl group on C3 may be present, the activating acetamido group in *p*-position may be made to prefer attack at C3. c) steric hindrance of *p*-acetamidophenyl group to addition at C3 may also play a role.

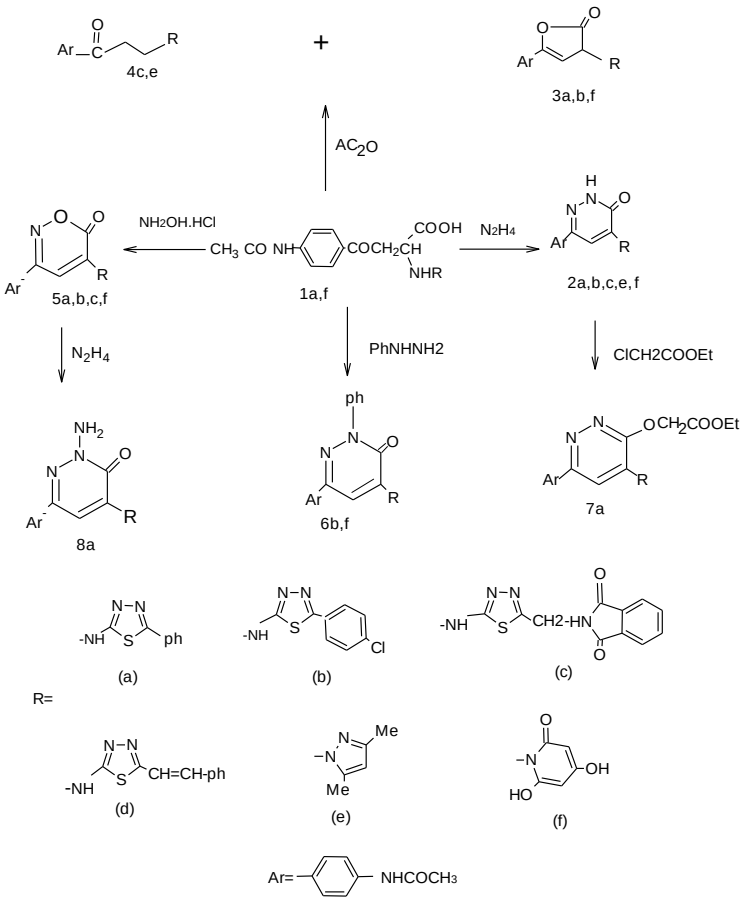
Since the entering nucleophile attacks C2 at expence of C3, so reasons 1 and 3 outweigh reason 2, in the preference of addition of an amino group to C2 of acids 1. The acids 1 are confirmed by spectroscopic tools, EIMS for acids 1 are 1a *m/z* 377 (M^+ - CO +H_2), 1_b *m/z* 358 (M^+ -(CO_2 +CH_2= CO) , 1c *m/z;* 446 (M^+-CO_2) , 1e *m/z:*307 (M^+ - H_2O). The explanation of one ^{1}HNMR spectrum for acids 1,*e.g.*, 1_b in DMSO exhibits signals at 2.5 (s,3H,CH_3CO),3.4 (2 dd , CH_2-C=O J=15.2, J=7.7) (diastereotopic protons) adjacent to ketonic group are non equivalent and each proton appears as douplet (4 lines, dd, J=15.2), each line couples with methine proton J=7.7 and gives two douplet of douplets (8 lines, 2 dd)), 4.2 (dd,CH-COOH,methine proton) 6.7 (s,NH),7.6-8.1 (m,8H,ArH) ArH),8.2 (s,1H,COOH),8.6 (s,1H,C=O-NH). It was reported[12] that the pyridazinone substituted 1,3,4- thiadiazolene were shown to be fungicidally active and their activity was influenced by the nature of the substituents. Thus, when acids 1 a-c were allowed to react with hydrazine hydrate in boiling ethanol, they afforded 6- acetanilido- 4 (5-aryl-2-amino 1,3,4 thiadiazole) 2,3 dihydro 3(2H) pyridazinones (2_{a-c}), not tetrahydropyridazinones[20]. The authors can explain auto-oxidation of initially formed tetrahydropyridazinones results dihydropyridazinone 2 due to the presence of activating aromatic moieties in position 4 enhancing the dehydrogenation of initially formed tetrahydropyridazinones , formation of extra conjugating system afforded more thermodynamic stable 2 . IR spectra of 2 a-c reveal strong absorption bands at 1630 cm^{-1} for υCO cyclic carboxamide and (3260 – 3270) for υNH whatever υ CO in phthalimido moiety in 2. EIMS for 2_a *m/z*:404 (M^+) , 2_b *m/z*: 403 (M^+-Cl) , 2_c *m/z* : 426(M^+- (CH_3+ H_2). The explanation of one ^{1}HNMR spectrum for Compounds 2, *e.g.*, 2_a revealed singlet at 2.5 assigned to methyl group, multiplet at 7.4 – 7.8 assigned for aromatic protons, singlet at 7.2 ppm for protons of pyridazinone, singlet at 10.2 assingned for two acidic protons of acetamido and pyridazinone moieties and singlet broad band at 6.5 ppm assigned for NH of thiadiazole moiety. Substituted pyrazole and barbiturate moieties constitute an important class of compounds in the field of agricultural and medicinal chemistry because of their broad spectrum biological activities[13] . Since, the combination of two or more heterocyclic and nonheterocyclic[14] systems enhances the biological profile more fold than their parent nuclei , so we considered to synthesize ; the pyridazinone has pyrazolyl and / or barbituryl groups in position 4 . Treatment of the acids $1_{e,f}$ with N_2H_4 in boiling ethanol, afforded 6-*(p*-acetamido phenyl)-4 (3,5-dimethyl pyrazolyl) and / or 2,4 - dihydroxy pyrimidinyl 6-one) 2,3,4,5 tetrahydro 3(2H) pyridazinone ($2_{d,e}$) . IR spectra of $2_{d,e}$ reveal strong absorption bonds at (1640 cm^{-1}) for υ CO of pyridazinone, EIMS for 2_d m/ z : 325 (M^+). Recently[15] 2 (3H) furanone exhibit rich photochemistry, furthermore, due to their common occurrence in nature, oxygen containing heterocyclic are frequent and important target, for synthesis

either as final products or as useful synthetic intermediate. Thus, when acids 1 was allowed to react with Ac2O on heating water bath for 1hr , they have 5(*p*-acetamido phenyl)-3-(5-aryl-2-1,3,4 thiadiazolylamino)-2-(3H) furanone (3_{a-b}) and/or 5(*p*-acetamidophenyl) -3 (2,4,6 dihydroxy pyrimidinyl -6-on)-2- (3H) furanone (3_f) . Their structures $3_{a,b,d}$ were inferred from IR spectra which exhibit strong absorption bands at (1767-1755 cm^{-1}) attributable to υ CO (lactonic) in addition to other carbonyl of acetamido gp at 1693 cm^{-1} . The ^{1} H NMR spectrum of compound 3a in DMSO exhibits signals at δ 2,1 (s, 3H, CH_3, CO), 4, (dd 1H,- C<u>H</u>-NH J=8.5) 7.5-7.9 (m,9H of Ar and 1H of furanone moieties), 6.7 (d,1H,NH,J=8.5), 12.7 (s,1H –C=O-N<u>H</u>) acidic protons exchangeable in D_2O. EIMS for compound 3_f m/z:343 (M^+). But interaction of acids $1_{c,e}$ with acetic anhydride afforded ketones 4. Formation of ketones 4 is due to the decarboxylation of acid $1_{c,e}$ *via* its heating at high temperature[16] presented as follow.



Here, the authors offer a speculation that stability of a zwitter ionic intermediate facile decarboxylation takes place in acids $1_{c,e}$. The presence of phthalimido and pyrazolyl groups which contain basic nitrogen enhances formation of a zwitter intermediate. IR spectra of 4 revealed absorption bands at (1706 cm^{-1}) corresponding to υ CO of ketones . EIMS for compound 4c, m/z ; 423 (M^+- CO). On the other hand, oxazinone derivatives are an important clan of heterocyclic compounds, since many of their heterocyclic system exhibit biological activity [17] . This promoted us to synthesize 1,2 oxazine derivatives incorporating with heterocyclic moieties in the position-5. Thus, the reaction of acids 1 with hydroxyl amine in refluxing pyridine, gave 3- (*p*-acetamido phenyl)-5- (5 aryl-2-amino-1,3,4thiadiazole and \or 2,4-dihydroxy-6-oxo pyrimidin-yl) 1,2 oxazin -6-one 5. Their structures were inferred from IR spectra which exhibit strong absorption bands at 1712-1703 cm^{-1} corresponding υ CO of azalactone irrespective CO for phthalimido and pyrimidinone moieties. EIMS for 5c m/z at 271 (M^+ -(Co_2+CH_2=C=O)) .The one of ^{1}H-NMR for oxazinone derivatives, 5_f in DMSO exhibits signals at 2.45 (s,3H,CH_3-C=O-), 7.0-7.4 (dd, 4H, phenyl group) , 8.0 (s,1H,oxazin (H 4)) , 6.9(s,2H, -C=O-CH_2-C=O- in barbiturate),8.3 (s,1H, pyrimidine moiety 1:1), 9.9 (s,1H,(OH NH) in pyrimidine = barbiturate equilibrium),12.5 (s,1H,-C=O-NH) of acetamido moiety. In the present work, treatment of acids 1 with phenyl hydrazine in boiling ethanol yielded 2-phenyl- 4- (5-

[*p*-chlorophenyl) 1,3,4 thiadiazol-2-amino] and/or 2,4-dihydroxy-6- oxopyrimidinyl) -6- (*p*-acetanilido) 3 (2H) pyridazinone 6 . IR spectra reveal strong absorption bands at (1632 cm^{-1}) corresponding to υCO in 6a and 1694-1650 cm^{-1} corresponding to two υCO of carbonyl of oxopyrimidinyl and pyridazinone moieties, respectively. Pyridazinone derivative 2a reacts with ethyl acetoacetate in the presence of potassium carbonate in dry acetone[18,19] to give 3(ethoxycarbonyl methoxy)-4- (5-phenyl–1,3,4 thiadiazol-2- amino)-6- acetanilido- 4,5- dihydro pyridazine 7. Its IR spectrum reveals strong absorption band for ester group , EIMS for compound 7 m/z: 492 corresponding to M^+ . Hydazinolysis of oxazinone derivative 5a by hydrazine hydrate in boiling ethanol afforded 2-amino- 4(5-phenyl 1,3,4 thiadiazol -2-amino) -6- (*p*-acetamidophenyl) 2,3dihydropyridazin-3-one 8 . IR spectra reveals strong absorption band at 1671 cm^{-1} corresponding to υ CO of carbonyl of pyridazinone moiety . The ^{1}H-NMR for compound 8 in DMSO exhibits signals at 2.5 (s,3H,CH3CO), 5.9-6.5 (m,3H,NH2&NH, which disappear in D_2O) ,6.9 – 7.6 (m,9H, Aromatic protons), 8.1 (s,1H, proton of pyridazine moiety), 12.5 (s,1H,CO-NH) which disappears by D_2O.



Experimental

All melting points are uncorrected.Elemental analyses were carried out at the Microanalytical Center, Cairo, Egypt. By Elementar Viro El Microanalysis, IR spectra (KBr) were recorded on infrared spectrometer ST-IR DOMEM Hartman Braun, Model: MBB 157, Canada and H-NMR spectra recorded on a varian 300MHz (Germany 1999) using TMS as internal standard. The mass spectra were recorded on Shimadzu GCMS-QP-1000 EX mass spectrometer at 70 e.v. Homogeneity of all compounds synthesized was checked by TLC.

General procedure of starting material

Anhydrous aluminium chloride (200 g) was added portionwise to a stirred solution of Maleic anhydride (100 g) in aromatic hydrocarbon, namely acetanilide (200 ml) in an ice bath. The whole mixture was stirred at room temperature for further 2 hr and refluxed for 3hr on water bath, then left to stand overnight. The participated solid after addition of ice cold hydrochloric acid (25 ml) was filtered off, dried and the crude product was crystallized form ethanol to give 3-*p*-acetamidobenzoyl-prop-2-enoic acid.

Formation of 3(p-acetamidobenzoyl)2-(5aryl 2-thiadiazolyl amino)propanoic acids (1a-d)

A solution of 3-(4-acetamidobenzoyl)-prop-2-enoic acid (0.01 mol) and 5-aryl-2-amino 1,3,4-thiadiazole (0.016 mol) in 30 ml ethanol was refluxed for 3hr. The crude product was washed by petroleum ether (b.p 40- 60^{o}C), and then, crystallized from ethanol to give compounds 1a,1b,1c or1d

Formation of 3-(p-acetamidobenzoyl)2-(5-(3,5 dimethyl)pyrazolo/or barbituro propanoic acid (1e,f)

A solution of 3-(4-acetamidoobenzoyl)-prop-2-enoic acid (0.01 mol) (2.55g) and 3,5 dimethyl pyrazole and /or barbituric acid 0.01 mole (1 g) in 30 ml ethanol in and then refluxed for 5 hr. The mixture was washed by light petroleum ether (b.p 40- 60^{o}C), and the solid was crystallized

Formation of 6-acetamidophenyl-4(5-aryl thiazolylamino,3 5 dimethyl pyrazolyl and /or burbituryl)-4,5-dihydro-3(2H)pyridazinones (2)

A solution of 1(0.01 mol) in ethanol (30 ml) was treated with hydrazine hydrate (0.75ml) and then refluxed for 4 hr. The solid that separated after concentration and cooling was recrystallized .

Formation of 5-acetamidophenyl-3-(5-aryl thiazolylamino, and /or burbituryl) furan-2-one (3 a,b,d,f)

A solution of $1_{a,b,f}$ (0.01 mol) and acetic anhydride (0.01 mol) (1 ml), was heated on water path for 1 hr. The product that separated on cooling was recrystallized from suitable solvent to give compounds 3a,b,d,f.

Formation of β-(5-phthalimido methyl thiazolylamino and/or 3,5 dimethyl pyrazolyl- 5-acetamido propiophenone (4 c,e)

A solution of $1_{c,e}$ (0.01 mol) and acetic anhydride (0.01 mol) (1 ml), was heated under reflux for 1 hr. The product that separated on cooling was recrystallized from ethanol to give compound 4c,e.

Formation of 3-acetamidophenyl-5(5-aryl thiazolylamino,3 5 dimethyl pyrazolyl and /or burbituryl)-4,5,6-trihydro-1,2-oxazine-6-one (5)

A solution of $1_{a,b,c,f}$ (0.01 mole) in pyridine (0.01 mol) (10 ml), was refluxed with hydroxylamine hydrochloride (0.01 mol) for 3 hr. The reaction mixture was left to cool then poured into cold water/HCl. The participated solid was filtered off and recrystallized from the suitable solvents to give compounds 5.

Formation of 6-acetamidophenyl-4(5-(4-chloro phenyl thiazolyl amino,and /or burbituryl)-1-phenyl-2,3-dihydro-3 (2H) pyridazinone (6 b,f)

A solution of 1b,f (0.01 mol) in ethanol (30 ml) was treated with phenyl hydrazine hydrate (1.4 ml) and then refluxed for 4 hr. The solid that separated after concentration and cooling was recrystallized from ethanol to give compounds 6.

Formation of 6-acetamidophenyl-4(5-phenyl thiazolylamino)-2-ethoxycarbonyl-methyl-2,3 –di hydropyridazine-3-one (7)

A solution of 2_a (0.01 mol) and ethylchloroacetate (0.01 mol) in dry acetone (20 ml), in the presence of potassium carbonate (3 g) was refluxed for 24 hr. The reaction mixture was concentrated, cooled and poured into ice cold water. The participated solid was filtered off, washed, dried and recrystallized from ethanol to give compound 7.

Formation of 1-amino -6-acetamido phenyl-4(5-phenyl thiazolylamino)- -2,3 - di hydro-3 (2H) pyridazinone (8a)

A solution of 5a (0.01 mol) and hydrazine hydrate (0.01 mol) ,was boiled in butanol (10 ml) for 3 hr. The reaction mixture was left to cool, then poured into cold water . The participated solid was filtered off and recrystallized from ethanol to give compound 8a.

TABLE 1. Characterization and physical data for synthesized compound.

Comp. No	M.P. °C.	Solvent of Cryst.	Formula M.W.	Analysis % calcd/found				
				C	H	N	Cl	S
1_a	190	Ethanol	$C_{20}H_{18}N_4O_4S$(410)	58.5 58.4	4.4 4.25	13.7 13.9	-	7.8 7.9
1_b	250	Ethanol	$C_{20}H_{17}N_4O_4SCl$(445)	53.9 53.7	3.8 3.7	12.5 12.7	8.00 8.23	7.4 7.4
1_C	210	Ethanol	$C_{23}H_{19}N_5O_6S$(493)	55.9 55.6	3.9 3.7	14.2 14.3	-	6.6 6.4
1_d	255	Ethanol	$C_{22}H_{20}N_4O_4S$(436)	60.5 60.4	4.6 4.5	12.8 12.7	-	7.3 7.3
1_e	254	Ethanol	$C_{17}H_{19}N_3O_4$(329)	62.0 62.2	5.9 5.7	12.9 12.8	-	-
1_f	300	Dioxan	$C_{16}H_{15}N_3O_7$(360)	53.3 53.2	4.3 4.2	11.7 11.7	-	-
2_a	190	Ethanol	$C_{20}H_{18}N_4O_4S$(410)	58.5 58.4	4.5 4.5	13.7 13.6	-	7.8 7.7
2_b	300	Ethanol	$C_{20}H_{17}N_6O_2SCl$(441)	54.4 54.4	3.9 3.8	19.0 18.8	8.00 7.87	7.3 7.5
2_c	270	Ethanol	$C_{23}H_{19}N_7O_4S$(489)	56.4 56.2	3.9 3.9	20.0 19.7	-	6.5 6.3
2_e	300	Ethanol	$C_{17}H_{19}N_5O_2$(325)	62.8 62.5	5.8 5.6	21.5 21.3	-	-
2_f	225	DMF	$C_{16}H_{15}N_5O_5$(357)	53.9 53.6	4.2 4.5	19.6 19.5	-	-
3_a	210	Dioxan	$C_{20}H_{17}N_4O_3S$(391)	61.5 61.4	4.3 4.2	14.3 14.3	-	8.3 8.2
3_b	300	Ethanol	$C_{20}H_{15}N_4O_3Cl$(427)	56.2 56.1	3.5 3.7	13.1 13.4	8.31 7.97	-
3_f	302	Ethanol	$C_{16}H_{13}N_3O_6$(346)	55.7 55.4	3.8 3.7	12.0 11.9	-	-
4_c	270	Dioxan	$C_{22}H_{20}N_5O_4S$(450)	58.7 58.4	4.4 4.2	15.5 15.2	-	7.1 6.8
4_e	280	Ethanol	$C_{16}H_{19}N_3O_2$(285)	67.3 67.1	6.7 6.4	14.7 14.3	-	-
5_a	255	Ethanol	$C_{20}H_{16}N_5O_3S$(406)	59.1 59.5	3.9 3.5	17.2 16.9	-	7.9 7.5
5_b	140	Ethanol	$C_{20}H_{15}N_5O_3SCl$(441)	59.4 59.7	3.4 3.6	15.9 15.5	8.05 7.78	7.3 7.5
5_c	282	Dioxan	$C_{23}H_{18}N_6O_5S$(490)	56.3 56.3	3.6 3.4	17.1 16.8	-	6.5 6.4
5_f	305	Ethanol	$C_{16}H_{13}N_4O_6$(357)	53.9 53.4	3.6 3.5	15.8 15.4	-	-
6_b	162	Ethanol	$C_{26}H_{20}N_6O_2S$(516)	60.5 60.2	3.9 4.2	16.4 16.7	-	6.2 6.3
6_f	220	Ethanol	$C_{22}H_{19}N_5O5$(433)	61.0 61.5	4.5 4.8	16.3 16.5	-	-
7_a	250	Ethanol	$C_{24}H_{24}N_6O_4S$(392)	58.5 58.8	4.9 4.3	17.1 17.4	-	6.5 6.2
8_a	302	Ethanol	$C_{20}H_{19}N_7O_2S$(421)	57.0 57.4	4.5 4.3	23.5 23.1	-	7.6 7.4

Biological Screening

The antimicrobial screening of all the synthesized compounds was done using the agar diffusion assay. This screening was performed against the Gram-positive bacteria, Gram-negative bacteria, *Staphylococcus aureus* Atcc 06538, *Escherechia coli* Atcc 10536, pathogenic fungi *Candida albicans* Atcc 1023 and *Aspergills flavus.* A moderate activity was observed with compounds which proved to possess marked activity against *E. coli, S. aureus* and *C. albicans*. The strong activity was observed with compound 6c.The inhibitory concentration was determined for each of the active compounds along with Tetracycline and Amphotericin as positive control. Activity was detected for the synthesized compounds except 1e, 3d and 4c toward *Aspergillus flavus*. Results are shown in the Table 2.

TABLE 2. Antibacterial and antifungal activities of some selected compounds.

Sample		***Escherichia coli*** **(G^-)**	***Staphylococcus aureus*** **(G^+)**	***Aspergillus flavus*** **Fungus**	***Candida albicans*** **Fungus**
Control : DMSO		0.0	0.0	0.0	0.0
Stan-dard	Tetracy-cline Anti-bacterial	32	30	–	–
	Ampho-tericin B Antifungal	–	–	16	18
1_a		14	14	12	10
1_b		14	14	14	12
1_c		15	14	14	12
1_d		14	13	14	11
1_e		14	13	0.0	0.0
3_b		13	13	13	10
3_d		14	15	0.0	10
4_c		13	14	0.0	0.0
5_b		13	12	13	12
6_c		16	16	13	12

Comp. No	**IR**	**NMR.(DMSO)**
1_a	υOH3410 υNH 3297- 3031,3050-2892 (C-H 1710) and (1680 cm^{-1}) acid and ketone groups	2.5(s,3H,CH_3CO),3.4(oct,CH_2.C=O J= 15.2,J=7.7) (diastereotopic protons) 4.2(dd,CH-COOH, methin proton J=7.7) 6.7 (s,NH),7.4-7.8 (m,9H,ArH), 8.2 (s,1H,COOH),8.6 (s,1H,C=O-NH)
1_b	υNH or OH 3150-3320 , 3050-2905 (C-H) 1710)and (1680 cm^{-1}) acid and ketone groups	2.5(s,3H,CH_3CO),3.4(oct,CH_2. C=O J=15.2 J=7.7)(diastereotopic proton) 4.2 (dd,CH-COOH, methin proton J=7.7) 6.7(s,NH),7.6-8.1 (m,8H,ArH), 8.2(s,1H,COOH), 8.6 (s,1H,C=O-NH)
1_c	υNHor OH 3327-3031,3055-2912(C-H (1770 – 1712 cm^{-1}) υCO phthalimido moiety, (1710) and (1680 cm^{-1}) corresponding to acid and ketone groups	2.45(s,3H,CH_3CO), 3.4(oct,CH_2C=O J=15.2,J=7.7) (diastereotopic protons) 4.1(dd,CH-COOH, methinproton J=7.7) 5.2 (s,2H,CH2) 6.2 (s,NH),7.4-7.8 (m,8H,ArH), 8.2 (s,1H,COOH), 8.6(s,1H,C=O-NH)
1_d	υNHor OH 3031-3297 , 3022-2912 (C-H (1710) and (1680 cm^{-1}) corresponding to acid and ketone group respectively.	2.5(s,3H,CH_3CO),3.4(oct,CH_2. C=O J=7.7) (J=15.2,diastereotopic protons) 4.2(dd,CH-COOH, methinproton J=7.7)5.3(d,1H,Ph-CHa=),5.6 (d,=CHb) 6.5(s,NH),7.4-7.8 (m,9H,ArH), 8.2(s,1H,COOH), 8.6 (s,1H,C=O-NH)
1_e	υNHor OH 3031-3297 (NH),3029-2892C-H (1710) and (1680 cm^{-1}) corresponding to acid and ketone group respectively.	2.7(s,9H,$3CH_3$),3.4(oct,CH_2. C=O J=7.7) (diastereotopic protons) ,4.2(dd,CH-COOH, methinproton J=7.7) 6.7(s,NH),7.2-7.6(m,5H,ArH), 8.2 (s,1H,COOH), 8.6(s,1H,C=O-NH)
1_f	υNHor OH 3450-3130, 3050-2900 (C-H (1710) and (1680 cm^{-1}) corresponding to acid and ketone group respectively and (1615) corresponding to barbiturate moiety.	2.5(s,3H,CH_3CO),3.4 (oct,CH_2. C=O J=7.7) (diastereotopic protons J=15.2) 4.2(dd,CH-COOH, methinproton J=7.7) 6.7(s,NH),7.1-7.5(m,6H,ArH), 8.2(s,1H,COOH),8.6 (bs,2H,C=O-NH) Acetamido and barbiturate moieties
2_a	υNH 3297-3125, 3055-2900 C-H (1640 cm^{-1}) for 2υ CO of amide group	2.5 (s,3H,CH3), 6.7 (s,NH) 7.4 – 7.8 (m,9H,ArH) 7.2 (s,1H,proton of pyridazinone, 10.2 (s,2H,NH acidic protons),
2_b	υNH 3270-3150, 3047-2882 C-H (1640 cm^{-1}) for 2υ CO of amide group	2.5 (s,3H,CH3), 6.7 (s,NH)7.4 –8.05 (m,8H,ArH) 7.2 (s,1H, proton of pyridazinone, 10.2 (s, 2H, NH acidic protons),
2_c	υNH 3300-3080, 3022-2912 C-H (1640 cm^{-1}) for 2υ CO of amide group (1772-1712)υ CO in phthalimido moiety	2.5 (s,3H,CH3), 6.7 (s,NH),6.8 – 7.9 (m,8H,ArH) 5.2 (s, 2H, CH2) , 7.2 (s,1H,proton pyridazinone), 10.2 (s,2H,NH acidic protons),

Comp. No	**IR**	**NMR. (DMSO)**
2_e	υNH 3297-3031 , 3060-2905 C-H (1640 cm^{-1}) for 2υ CO of amide group of pyridazinone and acetamido moietes	2.6 (s,9H,3CH3), 6.8 – 7.2 (m,4H,ArH) 7.5-7.6 (s,2H, protons of pyrazole and pyridazinone), 10.2 (s,2H,NH acidic protons),
2_f	υNH 3297-3120 , 3050-2912 C-H (1640 cm^{-1}) for υ CO of amide of pyrimidinonyl and pyridazinone moieties	2.3 (s,3H,CH3), 6.8 –7.3 (m,4H,ArH)7.5-7.8 (m,3H,protons of pyridazinone and pyrimidine moieties), 10.2 (s, 2H, NH acidic protons), 11.2(s,2H, OH)
3_a	υNH 3297-3100, 3055-2890 (C-H) 1767cm^{-1} attributable to υ CO lactonic and acetamido gp at 1693 cm^{-1}	δ 2,1 (s 3H, CH_3CO), 4(dd 1H, - C<u>H</u>-NH J=8.5), 6.7(bs,NH),7.5-7.9 (m,9H of Ar) , 6.9 (d ,1H,CH furanone moiety J=8.5) ,12.7 (s,1H –C=O-N<u>H</u>) acidic protons are exchangeable in D_2O,
3_b	υNH 3297-3031, 3022-2900 (C-H (1755 cm^{-1}) attributable to υ CO (lactonic) and acetamido gp at 1693 cm^{-1}	δ 2,1 (s 3H, CH_3CO), 4,(dd 1H, - C<u>H</u>-NH J=7.8),6.3(s,NH)7.0-7.9 (m,8H of Ar) , 6.7 (d,1H,CH furanone moiety J=7.8) ,12.2 (s,1H –C=O-N<u>H</u>) acidic protons
3_f	υNH 3297-3150, 3050-2912 (C-H (1760 cm^{-1}) attributable to υ CO (lactonic) and acetamido gp at 1693 cm^{-1}	δ 2,1 (s 3H, CH_3CO), 4.3(dd 1H, - C<u>H</u>-NH), 6.7(s,NH),7.5-7.9 (m,6H of Ar) , 6.7 (d ,1H,CH furanone moiety) , 12.2 (s,1H –C=O-N<u>H</u>) ,13.1(s,2H, OH)acidic protons exchangeable D_2O,
4_c	υNH 3300-3100 , 3050-2910 CH (1706 cm^{-1}) corresponding to υ CO of ketones	2.5 (s,3H,CH_3CO),3.4(t,CH_2.C=O J=7.7) 4.1 (t,CH_2.N J=7.7), 6.7 (bs,NH),7.0-7.8 (m,8H,ArH), 8.6(s,1H,C=O-NH)
4_e	υNH 3297 -30150, 3020-2912 (C-H3031-3297 ,3022-2912 (C-H (1706 cm^{-1}) corresponding to υ CO of ketones	2.4 (s,9H,3CH_3), 3.4 (t,CH_2C=OJ=7.7) (4.1 (t,CH_2N J=7.7), 6.7(bs,NH), 7.4-7.8 (m,5H, ArH and pyrazole moiety), 8.6 (s,1H,C=O-NH)
5_a	υNH 3297-3031, 3052-2912 (C-H1712-1703 cm^{-1} corresponding υ CO of azalactone	2.5 (s,3H,CH_3CO), 6.5 (s,NH),7.1-8.2 (m,10H, ArH and oxazine proton), 8.6 (s,1H,C=O-NH)
5_b	υNH 3240 -3111,3022-2912 (C-H1712-1703 cm^{-1} correspondin υ CO of azalactone	2.5(s,3H,CH_3CO), 6.7(s,NH),7.1-7.9 (m, 9H, ArH and oxazine proton), 8.6 (s,1H, C=O-NH)
5_c	υNH 3270-3030, 3060-2912 (C-H), υ CO of azalactone 1712-1703 cm^{-1} , υ CO at1772-1712 for phthalimido moieties	2.5(s,3H,CH_3CO), 5.2 (s,2H,CH2), 6.7 (s,NH), 7.1-7.9 (m,9H,ArH and oxazine proton), 8.6(s,1H,C=O-NH)
5_f	υNH 3290-3100, 3050-2912(C-H) 1712, 1703,1683 cm^{-1} υ CO of azalactone, υ CO barbituro and pyrimidinone moieties	2.5(s,3H,CH_3CO), 6.7(s,NH),6.9-8.3 (m,8H, ArH Pyrimidine and oxazine protons),), 9.9 (bs,1H,OH acidic proton and 12.4 (s,1H,C = ONH are exchangeable in D_2O,)

Comp. No	IR	NMR. (DMSO)
6_b	υNH3131-3410,CH 3022-2912,υCO 1632 cm^{-1}) and 1694-1650 corresponding to υ CO of carbonyl pyridazinone moieties.	2.5 (s,3H,CH3), 6.5(s,NH)6.8 – 7.9 (m,13H, ArH) ,8.2(s,1H,proton of pyridazinone, 10.2 (s,1H,NH acidic protons),
6_f	υNH3031-3297),CH 3022-2912, 1694-1650 cm^{-1} corresponding to 2υ CO of carbonyl of pyrimidinonyl and pyridazinone moieties	2.3 (s,3H,CH3), 7.0 –7.8 (m, 9H, ArH) 8-8.2(s,3H,protons of pyridazinone and pyrimidine moieties, 10.2 (s,1H,NH acidic protons), 11.2 (s,2H, OH)
7_a	υNH 3031-3297 , CH 3022-2912 υ CO 1741 cm^{-1} of ester	1.3(t,3H,CH3,J=7.4), 2.5 (s,3H,CH_3CO), 3.4 (q,2H, CH_2. J=7.4), 4.8 (s,2H,CH2 6.7 (s,NH), 7.0-7.8 (m,10H,ArH and proton of pyridazinone) 8.2 (s,1H,COOH),8.6 (s,2H,NH-C=O)
8_a	υNH 3031-3297 , 3022-2912 (C-H1671 cm^{-1} corresponding to υ CO of carbonyl of pyridazinone moiety	2.5 (s,3H,CH3CO), 5.9-6.5 (m,3H, NH2 & NH, disappear in D_2O) ,6.9 – 7.6(m, 9H, aromatic protons), 8.1 (s,1H, proton of pyridazine moiety), 12.5 (s,1H,CO-NH) disappears by D_2O .

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استخدام البارا اسيتاميدوبنزويل حمض البروبينويك في تحضير احماض امينية جديدة و استخدامها لتحضير مركبات غير متجانسة الحلقة

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يتضمن هذا البحث 1- تحضير بعض الاحماض الامينية الصناعية التى لها نشاط بيولوجى . وذلك من خلال معالجة حمض 3-(4-اسيتاميدو بنزويل)-2-البروبينويك مع 5-اريل-2-امينو-1,3,5ثياديزول و 2,5-ثنائى الميثيل البيرازول و حمض البربيتيوريك للحصول على ناتج الاضافة(1).الذى يستخدم لتحضير العديد من المركبات الغير متجانسة الحلقة هثل البيريدازينون و الاكزازينون والفيورانون . 2-اجراء بعض التحاليل البيولوجية لاثبات فاعلية هذة المركبات ضد بعض الامراض البكتيرية و الفطرية .3-اثبات المركبات المحضرة بأجهزة التحاليل الدقيقة مثل الاشعة تحت الحمراء والرنين المغناطيسى والكتلة الاكترونى.